Diagn Interv Radiol 2015; 21:85–92

NEUROⅯRADIOLOGY

ORIGINAL ARTICLE

Functional MRI compliance in children with attention deficit hyperactivity disorder

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PURPOSE
We aimed to test the effect of prescan training and orientation in functional magnetic resonance imaging (fMRI) in children with attention deficit hyperactivity disorder (ADHD) and to investigate whether fMRI compliance was modified by state anxiety.

METHODS
Subjects included 77 males aged 6–12 years; there were 53 patients in the ADHD group and 24 participants in the healthy control group. Exclusion criteria included neurological and/or psychiatric comorbidities (other than ADHD), the use of psychoactive drugs, and an intelligence quotient outside the normal range. Children were individually subjected to prescan orientation and training. Data were acquired using a 1.5 Tesla scanner and an 8-channel head coil. Functional scans were performed using a standard neurocognitive task.

RESULTS
The neurocognitive task led to reliable fMRI maps. Compliance was not significantly different between ADHD and control groups based on success, failure, and repetition rates of fMRI. Compliance of ADHD patients with extreme levels of anxiety was also not significantly different.

CONCLUSION
The fMRI compliance of ADHD children is typically lower than that of healthy children. However, compliance can be increased to the level of age-matched healthy control children by addressing concerns about the technical and procedural aspects of fMRI, providing orientation programs, and performing on-task training. In patients thus trained, compliance does not change with the level of state anxiety suggesting that the anxiety hypothesis of fMRI compliance is not supported.

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Received 16 January 2014, revision requested 5 March 2014, final revision received 13 August 2014, accepted 14 August 2014.

Published online 17 December 2014.
DOI 10.5152/dir.2014.14006

Functional magnetic resonance imaging (fMRI), which uses blood oxygen level-dependent contrast, is a noninvasive procedure for imaging regional brain activity. MRI exhibits high spatial resolution; even 1.5 Tesla (T) imaging used in standard clinical practice (spatial resolution of 2–4 mm) yields robust functional signal changes (1). MRI can be performed without the ethical concerns associated with the other available imaging techniques and can thus be used in children and in healthy populations. In healthy volunteers, fMRI has produced reproducible findings across scanning sites and age groups with respect to the localization and development of cognitive processes (2). Its capacity for noninvasive imaging of the brain *in vivo* during cognitive processing has made fMRI an exciting tool for laboratory research, as well as clinical studies and clinical practices that involve diagnosis, follow-up, and presurgical mapping (3, 4).

A disorder that attracts a great deal of attention in children is attention deficit hyperactivity disorder (ADHD). This focused attention is partly due to the high incidence (0.2%–12.2%) of ADHD, which is also the most frequent diagnosis in children referred to child psychiatry departments (5–7). From the neuropsychological point of view, ADHD is associated with deficits in executive functions (8, 9). Nevertheless, as the number of theories on the subject demonstrates, ADHD remains an unresolved issue, especially with respect to its biological basis and brain correlates (10).

With its many merits, fMRI would be a valuable tool for studying the etiology, diagnosis, and follow-up of ADHD patients. However, MRI is movement-sensitive, and movement artifacts impair the diagnostic quality of the examination and can even render the scans unusable. A meta-study involving 21 000 cases, reported an overall artifact frequency of 40% (11). Normal body pulsations accounted for 7%–12% of the artifacts, but at least 10% were due to motoric unrest or restlessness. In another study, artifacts other than normal body pulsations were reported in 12.8% of the scans and 6.4% of the scans were impaired in diagnostic quality (12).

The symptoms of ADHD include hyperactivity, impulsivity, and inattention (13). Of these symptoms, the first two directly challenge the immobility requirement of MRI, and the third poses a problem for the task-appropriate responses that cognitive tasks require for functional imaging. Not unexpectedly, the fMRI compliance of ADHD patients is poor. In 7–12-year-old unmedicated ADHD patients, the frequency of successful runs was 77%, and the success rate for the completion of the total fMRI battery was 50%, while the values for age-matched healthy volunteers were 96% and 88%, respectively (14).

Artifacts other than those caused by organ pulsations have been associated with anxiety or anxiety-sensitivity (15). Medium-to-severe anxiety was reported in 25%–37% of adults undergoing MRI (16, 17). Up to 30% exhibited anxiety-related reactions that ranged from apprehension to a reaction level severe enough to interfere with performance (18). MRI artifacts were also related to the degree of fear and/or panic and anxiety disorders such as claustrophobia (16, 19).

A group of studies rejected the contribution of anxiety and proposed another set of causal factors for the artifacts and the resulting fMRI incompliance. According to these studies, patient distress can be predicted from the degree of claustrophobia but not from anxiety sensitivity *per se* (16). An analytical study (12) measured state anxiety using the Spielberger State-Trait Inventory (STAI), a tool commonly used for measuring state anxiety (20). In their study, state anxiety did not account for the development of movement artifacts. The artifacts were found to be associated with prescan concerns about the technical apparatus and with the procedural aspects of imaging; these concerns were focused on the narrowness of space, noise, immobility, and scan duration. The concerns, which were rated as hardly bearable, were identified in 70.6% of all individuals developing movement artifacts.

An approach for meeting the concerns about the technical and procedural aspects focuses on patient comfort and cooperation. In ADHD patients, the effect of individualized prescan preparation was investigated using operant-contingency-based procedures where immediate verbal feedback was provided on response accuracy and where positive reinforcement (verbal praise) was delivered upon criterion achievement (21). This prescan preparation reduced the extent of head movements in both ADHD patients and healthy controls. However, the approach was time-consuming and, due to the sample size (n= 4), too small to be generalizable. Another approach adopted a systematically administered prescan orientation and training program (22). The study reported an overall success rate of approximately 80% in normal children and adolescents (age range, 5–18 years). Based on these findings, the study concluded that it is feasible to conduct large-scale fMRI studies in children. To our knowledge, the effect of such prescan preparations on fMRI compliance has not yet been investigated in children with ADHD.

Table 1. Descriptive statistics on study groups

	Sample size	Age (months) Mean	SEM
ADHD-AD	16	120.13	3.95
ADHD-C	37	113.27	3.11
Control	24	119.58	3.36
Total	77	116.66	2.01

SEM, standard error of the mean; ADHD-AD, attention deficit hyperactivity disorder subtype characterized predominantly by attention deficit; ADHD-C, attention deficit hyperactivity disorder combined subtype.

In this study we aimed to demonstrate whether prescan training and orientation affect fMRI compliance of children with ADHD and determine whether this compliance is modified by state anxiety. The study used a well-known cognitive task in the neuropsychology literature, with well-documented activation patterns in the brain.

Methods

Subjects

The present study reports findings on a section of a large-scale project (HUAF-BAB 2006K-120-640-06-08) using multiple technologies. This study used a subsample (53 boys with ADHD and 24 boys in the control group) of the larger study protocol (70 boys with ADHD and 38 boys in the control group).

ADHD patients were clinically referred or were recruited from schools via teachers and parent support groups. Diagnosis and subtyping was based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders-IV (13) and the Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Present and Lifetime version (23). The latter tool was also used in checking for comorbidities. In both tools, the informants were the parents. Due to the small percentage of patients having the subtype characterized predominantly by hyperactivity and impulsivity (HI), the clinical sample consisted of the subtype characterized predominantly by attention deficit (ADHD-AD) and the combined subtype (ADHD-C) (Table 1). All patients were unmedicated first referrals.

Participants in the clinical and control groups were 6–12 years of age and were enrolled in the respective age-relevant grades of primary school. Table 1 presents the number of participants and descriptive statistics on age. Age distribution of the groups was homogeneous with no statistically significant difference between the groups (One-way Analysis of Variance [ANOVA], $F[2,74]= 1.331$, $P = 0.270$; Levene's test, $P = 0.502$).

The exclusion criteria for clinical and control groups were a history of psychiatric and/or neurological dysfunction (other than ADHD), the use of drugs that can alter cognitive functioning, uncorrected visual and/or auditory impairments, Full Scale Intelligence Quotient outside the normal range (<90 or >130) and a clinical level depression on the Kovacs Depression Inventory for Children.

The nature of the study was fully explained to the parents. Volunteering parents signed an informed consent form, according to the institutional regulatory criteria. Oral assent from the children was another requirement for participation. Institutional approvals were obtained.

Study procedure

Anxiety was measured using the Spielberger State-Trait Anxiety Inventory (STAI) which was administered in the hospital setting before MRI. Preparation and training for the fMRI scan consisted of several steps that were conducted on the day of the scan. Children and their parents arrived in the Radiology Department and were met by the study coordinator. Children were taken on a tour of the department during which the MRI scanner and other data acquisition devices were shown and explained. Children were introduced to a fixed group of staff and technicians who were responsible from the data acquisition procedure. They were allowed to watch as another child was being scanned and were meanwhile given the opportunity to ask questions. They were treated with reinforcers such as candy bars, chocolate sticks, and story books and were allowed to choose the one they liked.

Just before MRI, a standard training session was conducted outside the scanner in a room suitable for psychometric testing. Children were individually trained on a short version of the task. Practice trials were repeated until the children understood the task and what was required of them for performing the task. In case of incorrect and/or inappropriate responses, the task was re-explained, and training was continued. Training was terminated when accuracy level was stabilized, demonstrating that the patient was working at the limits of his capacity.

After careful preparation, the child was escorted by an MRI technician and a psychologist to the magnet room. MRI was performed within a research time using equipment specifically dedicated to the study. While in the magnet room, the child was systematically introduced to the equipment; the scanner, head coil, headphones, and response pads. When the child was ready and there were no overt signs of distress, scanning started. Structural scans were performed before the functional scans. A time interval of at least 45 min was allowed to pass between the structural and functional scans, during which, the child was allowed to engage in leisurely activities.

Task procedures

We used one of the two neurocognitive tasks from the TURCONS neuropsychological mapping battery for fMRI (1). The tasks were presented to the children in an alternating order. Block-design tasks began with leading acquisitions (dummy) that were discarded to exclude early signal decay and to ensure that brain magnetization has reached a steady state before task presentation.

The stimulation task was modified from the Stroop test. The Stroop test measures complex attention that consists of selective attention, focused attention and interference control (24, 25).

The Stroop test began with three leading acquisitions (3000 ms black screen + 2000 ms screen instruction screen, + 3000 ms black screen). The Stroop test consisted of four task blocks (words) and four control blocks (circles) that were presented in alternating order. The task block consisted of congruently or incongruently colored words. The control block consisted of a pair of congruently or incongruently colored circles. There were 15 words (or pair of circles) in each block (altogether 15×4=60). Each color word (or pair of circles) was presented for 1350 ms. The inter-stimulus interval was filled with a black screen and was 2000 ms in duration. The child was asked to press the response pad button that coincided with the index finger when the color word (or pair of circles) was congruent and to press the button that coincided with the middle finger when they were not congruent. The total duration of the run was 4.08 min.

Behavioral data (number of correct responses and reaction times) were collected as the child performed the Stroop task while inside the scanner.

Imaging parameters and data analysis

The stimuli and the task were prepared and presented using the Stim2 software (Neuroscan, Compumedics, Charlotte, North Carolina, USA). Visual stimuli were transmitted over fiber optic cables to a projector (Silent Vision 6011, Avotec, Stuart, Florida, USA) situated in the MRI scanner room and from there to a transparent screen that was affixed to the bore of the scanner. The visual image on the screen was then projected to a mirror that was attached to the head coil. Finger-press responses were recorded using a two-button MRI-compatible response pad (LU-444RH, Lumina, Cedrus, San Pedro, California, USA). Head movement was restrained using foam padding on either side of the head.

Data were acquired with a 1.5 T superconducting MRI system (Signa Excite 11x; GE Medical Systems, Milwaukee, Wisconsin, USA) using an 8-Channel domed design diagnostic head coil (800152, GE Hi-Res Head Coil, InVivo Corporation, Gainesville, Florida, USA). Maximum gradient strength and slew rate of the scanner was 33 mT/m and 120 mT/m/s, respectively. The sensitive volume of the head coil was 24 cm in the superior/inferior direction with increased signal-to-noise ratio throughout. Table 2 presents the imaging protocol for structural and functional imaging. The total duration of a single functional session was approximately 20 minutes including the necessary localizer, masking, functional, and structural sequences.

Fast spin echo (FSE) T1-weighted images at the sagittal plane were used for localizing the anterior commissure/posterior commissure plane. The structural and functional data series were analyzed using Brain Voyager software (versions 2.0 and QX2.9) (Brain Innovations, Maastricht, the Netherlands). The inhomogeneities in the structural data were corrected using SPM-8 (Wellcome Trust Centre for Neuroimaging, London, UK).

The functional data series of each participant from each stimulation task were preprocessed for the mean intensity adjustment, slice scan time correction (correction with sinc interpolation, slice scanning order ascending interleaved), three-dimensional (3D) motion correction (using trilinear/sinc interpolation), spatial smoothing and temporal filtering (smoothing with Gaussian filter and temporal high-pass with three cycles per points). Except in the case of the 3D motion correction, preprocessing used the default options of Brain Voyager 2.0. The cutoff value for rejecting data for excessive head motion was 1 mm. After 3D motion correction, translation and rotation values were observed to be less than 1 mm for the neurocognitive Stroop task (Table 3).

After preprocessing the functional data and concatenating it with the boxcar function, the functional series of each participant were coregistered with two structural image series (one of which was low resolution and the

Table 2. Structural and functional imaging protocols

No	Sequence definition	Sequence type	Weighting	TR	TE	FA	ST	SI	SN	AT	FOV	Matrix	NEX
Structural imaging													
1	Primary localizer	GE	T1	Auto	Auto	Auto	3.0	1.0	5	0:33	28	256×128	2
2	Secondary localizer	FSE	T1	500	11.8	-	3.0	0.3	8	1:14	20	320×192	3
3	3D structural	SPGR	T1	Auto	Min	20	1.0	0.0	172	13:04	24	256×160	3
4	General scanning	FRFSE	T2	2950	100	-	5.0	2.0	20	2:15	24	512×224	2
5	Masking	FRFSE	T2	3240	96	-	6.0	1.0	11	1:51	28	512×512	1
Functional imaging													
No	Sequence definition	Sequence type	Weighting	TR	TE	FA	ST	SI	SN	AT	FOV	Matrix	NEX
1	Primary localizer	GE	T1	Auto	Auto	Auto	3.0	1.0	5	0:33	28	256×128	2
2	Secondary localizer	FSE	T1	500	11.8	-	3.0	0.3	8	1:14	20	320×192	3
3	Masking (first)	FRFSE	T2	3250	85	-	6.0	1.0	11	1:50	28	512×512	1
4	Functional (WCST)	EPI	T2*	3000	60	90	6.0	1.0	11	4:36	28	128×128	1
5	Functional (STROOP)	EPI	T2*	3000	60	90	6.0	1.0	11	4:36	28	128×128	1
6	Masking (second)	FRFSE	T2	3250	85	-	6.0	1.0	11	1:50	28	512×512	1
7	3D structural	SPGR	T1	Auto	Min	20	3.0	0.0	60	5:04	24	256×256	2

TR, time of repetition; TE, time of echo; FA, flip angle; ST, slice thickness; SI, interslice interval; SN, number of slices; AT, acquisition time; FOV, field of view; NEX, number of excitation; GE, gradient echo; FSE, fast spin echo; SPGR, spoiled gradient recalled; FRFSE, fast recovery fast spin echo; EPI, echo planar imaging; 3D, three-dimensional.

Table 3. Mean and standard error of translation and rotation of head movements during functional imaging for the Stroop test

	Translation (mm)						Rotation (degree)					
	x		y		z		x		y		z	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
ADHD-AD	0.12	0.08	-0.01	0.04	0.12	0.25	0.11	0.11	-0.15	0.10	-0.22	0.07
ADHD-C	0.04	0.05	0.07	0.03	0.24	0.07	0.28	0.08	0.01	0.03	-0.19	0.05
ADHD-Total	0.06	0.04	0.05	0.03	0.21	0.08	0.24	0.07	-0.03	0.04	-0.20	0.04
Control	-0.05	0.78	0.07	0.03	0.33	0.09	0.25	0.11	0.04	0.04	-0.27	0.07

SEM, standard error of the mean; ADHD-AD, attention deficit hyperactivity disorder subtype characterized predominantly by attention deficit; ADHD-C, attention deficit hyperactivity disorder combined subtype.

other high resolution) to obtain a 4D data set in which space (x, y, z) and time (functional series) were united. Analyses were performed using Brain Voyager QX 2.9. For each person and paradigm, the preprocessed 4D data were analyzed with a general linear model to obtain task-generated activations/deactivations for single participants. In doing this, hemodynamically (two gamma) convolved task blocks served as boxcar predictors. Activation areas were defined at a threshold value of ≥50 jointly activated voxels in a specific region-of-interest. False discovery rate was set at q=0.05. To determine the corresponding Brodmann areas (BAs), Lancaster's Talairach Deamon was used to transport all Talairach coordinates in given clusters into text files. Because the nearest grey matter option gave a vast number of voxels for a given BA in the Deamon, the single-point option was selected as the sorting criterion. The resulting Talairach-normalized mapped td.txt files were transported to Excel 2010. These were then filtered and averaged for selected BAs. Individual BAs were localized using the Talairach coordinates with highest t and *P* values.

Evaluation of compliance

MRI compliance was assessed through scan success, scan failure, and repetition rates. The success rate was calculated as the frequency of the total number of children completing the total fMRI protocol with an acceptable amount of head motion (14). Scans that were repeated due to movement artifacts were not included in the successful category. The failure rate was the frequency of scanning sessions that had to be cancelled due to refusal to enter the scanner, request for exiting the scanner, refusal to begin or finish the runs after entering the scanner, expression of distress while in the scanner and excessive head motion (22). Scan failures due to non-task factors or technical problems were not counted in the failure category. The repetition rate pertained to the number of scanning sessions that had artifacts, were repeated and were successful upon repetition.

Table 4. Outcome of structural and functional scans

	ADHD-AD	ADHD-C	Control	*P**
Structural scans				
Success rate	13	36	23	0.080
Failure rate	15	37	24	0.145
Repetition rate	14	36	23	0.324
Functional scans				
Success rate	9	17	14	0.593
Failure rate	16	34	22	0.496
Repetition rate	9	20	16	0.609

*Pearson chi-square test.
ADHD-AD, attention deficit and hyperactivity disorder subtype characterized predominantly by attention deficit; ADHD-C, attention deficit and hyperactivity disorder combined subtype.

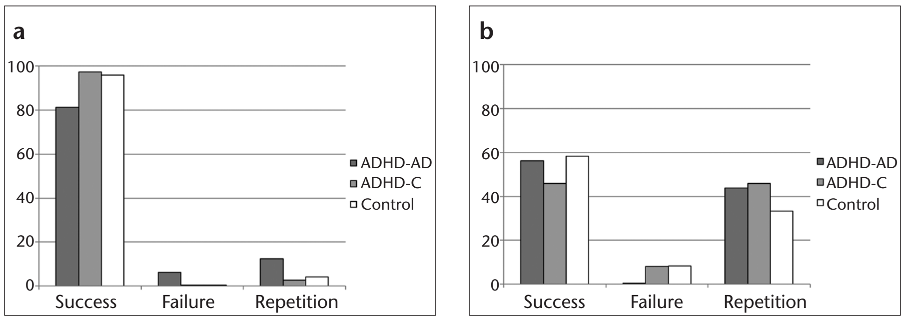

Figure 1. a, b. Success, failure, and repetition rates in structural **(a)** and functional **(b)** scans for ADHD-AD, ADHD-C, and control groups.

Statistical analysis

Correct responses to Stroop test and reaction times were compared between groups using multivariate ANOVA. Compliance was analyzed separately for the structural and functional scans for the three indices of fMRI compliance (assessed as success, failure, and repetition rates). The significance of the relationships among the groups and indices of fMRI compliance was tested using a three-sample Pearson chi-square test. The significance of the relationships between the indices of fMRI compliance and the anxiety level was tested using a two-sample Pearson chi-square test. Fisher's exact test was used when the expected frequencies were less than five. State anxiety scores were confirmed to follow normal distribution by Kolmogorov-Smirnov test ($P = 0.206$) and extreme samples analysis was performed to establish the difference between patients with low (at or below 25th percentile) and high (at or above the 75th percentile) anxiety scores. The limit of significance was set at 0.05.

Results

The number of behaviorally correct responses that was obtained from the ADHD cases as they performed the Stroop test throughout fMRI was lower than that obtained for the control group (control group, 26.4±2.1 correct responses; ADHD group, 24.1±4.5 correct responses). Pairwise comparison of the two groups by multivariate ANOVA showed that the number of correct responses of the healthy controls were significantly higher than that of the ADHD cases ($F[1,70]=4.828$, $P = 0.031$, eta=0.066). The reaction times of the two groups were not significantly different.

MRI compliance was separately analyzed for structural and functional scans. Fig. 1 demonstrates the percentage of success and failure rates and the percentage of scans that were repeated due to artifacts. A consistent profile was not observed in either structural or functional scans. In the structural scans (Fig. 1a), the highest success rate (95.8%) belonged to the control group. The control group and the ADHD-C group showed no failure (0%). The difference in compliance between the groups ceased to exist in the functional scans (Fig. 1b). The control group shared a similar success rate with ADHD-AD group (58.3% and 56.2%, respectively) and had the highest failure rate (8.3%). The repetition rate did not exhibit a consistent trend in the structural and functional scans or between subtypes of ADHD and the control group.

Considering the entire study population (n=77), a higher overall compliance was observed in the structural scans in comparison to the functional scans. In the structural scans, success rate was higher (93.5% vs. 52.0%), failure rate was lower (1.3% vs. 6.5%) and repetition rate was also lower (5.2% vs. 41.6%).

For both structural and functional scans, frequencies pertaining to indices of compliance were equally distributed among subtypes of ADHD and control groups. Success, failure, and repetition rates did not significantly differ between the clinical and control groups (Table 4).

As previous analyses did not reveal a significant difference between the fMRI compliance of the two subtypes of ADHD, analyses pertaining to the effect of anxiety were performed without subtype differentiation. State anxiety scores ranged from 20 to 58. The anxiety scores at the 25th and 75th percentiles were 25 (n=13) and 35 (n=11), respectively. Mean anxiety score was 23.2±1.6 for the low anxiety group and 44.4±7.6 for the high anxiety group. State anxiety was significantly different between high and low anxiety groups ($P < 0.001$).

Fig. 2 demonstrates the success and failure rates and the percentage of scans that were repeated due to artifacts for low and high state anxiety during structural and functional tests.

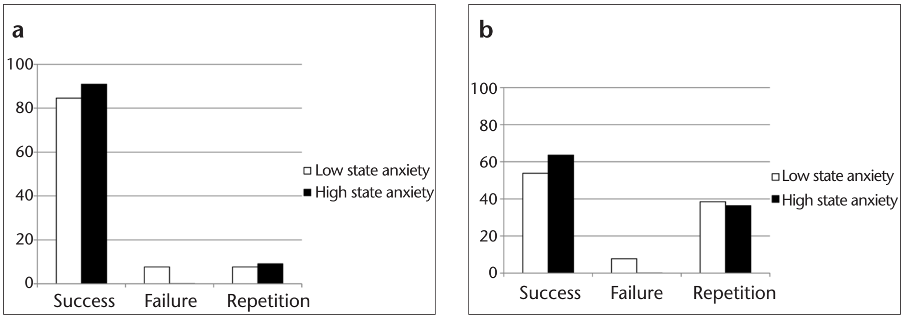

Figure 2. a, b. Success, failure, and repetition rates in structural **(a)** and functional **(b)** scans for extremes of anxiety in the ADHD group.

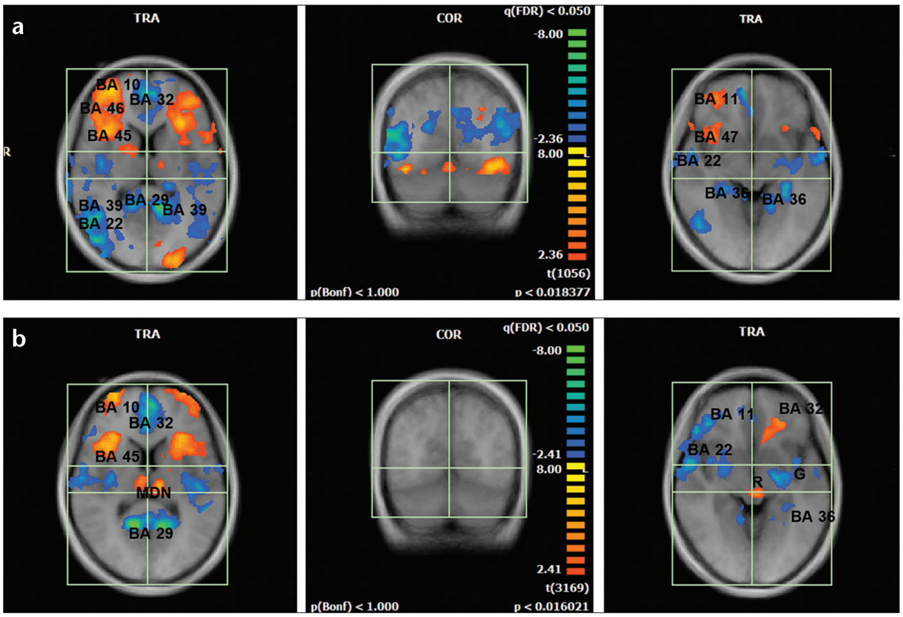

Figure 3. a, b. Group activation maps for the Stroop task in the healthy control group **(a)** and the ADHD group **(b)**.

No significant relationship was found between the states of anxiety and fMRI compliance in structural or functional scans, demonstrating that the success, failure, and repetition rates did not differ significantly between the extremes of state anxiety in ADHD patients.

Fig. 3 presents the group averages of the activation maps of ADHD and control groups on the Stroop task. The general pattern in healthy control children was distributed activation in the frontal lobes and deactivation in the posterior brain. The activations were focused in the orbitofrontal cortex and the motor speech centers (BA 44–46), and deactivation was localized to the anterior and posterior cingulate, angular gyrus, and Wernicke's area. Deactivation was not as pronounced in ADHD patients who, unlike healthy control children, exhibited activation at the dorsomedial nucleus of the thalamus as well.

Discussion

The present feasibility study aimed to investigate the effectiveness of a prescan training and orientation program on the fMRI compliance in children with ADHD. Compliance was measured through success, failure, and repetition rates. The performance of the ADHD group was compared to that of the healthy age-matched control group. There was no significant difference between ADHD and control groups in terms of fMRI compliance. Moreover, there was no significant difference between the low- and high-state anxiety ADHD groups with respect to any of the compliance indices.

The behavioral findings showing a lower number of correct responses in the ADHD group are concordant with the literature (10). The activation patterns that the stimulation task produced in healthy control children are also in line with the related literature. The frontal activation and posterior deactivation supports the anterior and posterior selective attention systems of the brain (26). The prefrontal activation with a focus on the orbitofrontal cortex (27) and another at the anterior cingulate cortex supports the literature that distinguishes the roles of these two regions in Stroop performance and cognitive control (1, 28, 29). The less extensive activation in the frontal lobes coupled with the activation in the dorsomedial nucleus is in line with the executive dysfunction in ADHD, showing that, in ADHD, the brain tries to manage the executive function normally associated with the frontol lobe, with subcortical structures (8, 9). Less extensive deactivation in ADHD is consistent with the problems that these patients have with respect to selective resource allocation (10).

In fMRI, compliance of children with ADHD is appreciably lower than that of age-matched healthy controls (14). The lower rate of successful runs (ADHD, 77%; control, 96%) is expected based on the symptoms of hyperactivity and impulsivity, which potentially lead to movement artifacts. The lower rate of task completion (ADHD, 50%; control, 88%), on the other hand, is expected on the basis of inattention, which potentially leads to lower task-related performance during fMRI (14).

Our study addressed the fMRI compliance problem of ADHD patients using an approach that Byars et al. (22) developed for normal children and adolescents, where technical and procedural concerns are treated using individualized orientation and training programs on the day of the scan. In their study, the average failure rate in normal male children was 8.5% (normal male children and adolescents had an overall success rate of 74%). We found a comparable failure rate of 8.3% in our control group, showing that the effect of the prescan program on fMRI compliance of the normal control subjects in the present study is analogous to that of Byars et al. (22).

Yerys et al. (14) study on the fMRI compliance of children with ADHD (n=52) showed 50% overall success rate for completion of an fMRI battery. There was a wide difference between the success rates of ADHD group and the typically developing age-matched children (88%). In our study, the success rate of healthy control males was 58.33%, while those of unmedicated ADHD-C and ADHD-AD patients were 46.0% and 56.2%, respectively. These findings suggest that the prescan intervention decreased the difference between the ADHD and control groups and brought fMRI compliance of the ADHD patients up to the level of healthy controls. According to this finding, individualized orientation and training makes fMRI possible in hyperactive, impulsive, and inattentive ADHD cases. Accordingly, large-scale fMRI studies can be conducted not only in normal children (22), but also in cases with ADHD.

State anxiety is a normal physiological response of the autonomic nervous system. Caused by an outside factor, state anxiety is associated with a temporary change in a person's emotional state. State anxiety varies in intensity and fluctuates over time (20). The technical and procedural aspects of fMRI, as well as the significance and probable outcome of the fMRI report may provoke stress and stress anxiety (30). Indeed anxiety sensitivity, anxiety-related reactions, fear, panic, and claustrophobia lead to movement artifacts and negatively affect fMRI compliance (15–17). As a result of such studies, anxiety, particularly state anxiety, has been treated as a determinant of fMRI compliance.

In this study, state anxiety scores of the ADHD patients were normally distributed, with low and high scores on the symmetrical extremes of the normal curve. The differences between the anxiety scores of these extreme groups were significant. However, differences between the success, failure, and repetition rates (the three indices of fMRI compliance) of the extreme anxiety groups were not significant. Our findings support the findings of Dantendorfer et al. (12), who also failed to find an association between STAI-measured state anxiety scores and fMRI compliance. These findings suggest that the anxiety hypothesis of fMRI artifacts and compliance is not plausible.

An original finding of the present study was the compliance difference between the structural and functional scans (success rates of 93.5% and 52.0%, respectively). The visual task (Stroop) that was used in our study produces eye movements and, during visual scanning of the Stroop stimuli, head movements. The task requirements in fMRI also lead to alertness (30); such an arousal state is usually accompanied with other indexes of arousal, one of which is increase in muscular tonus. All of these factors are artifactual in nature and they thus serve to reduce the success rate in functional scans. In structural scans, on the other hand, subjects passively listen to self-chosen music or to stories. These conditions produce relaxed wakefulness, an arousal state that is conducive to immobility, and resultantly, to high success rate. These speculations should obviously be analytically investigated in future studies. However, our findings point out that, in children who receive prescan orientation and training program, compliance is an issue in functional but not in structural MRI.

A limitation of our study is the gender of the study sample. ADHD occurs more frequently in males than females; the values vary between 2:1 and 6:1 (31, 32). Due to this selective predominance, our study was conducted on males only. Future studies should investigate the effect of prescan orientation and training program on MRI compliance of females, especially since Byars et al. (22) found a higher success rate in normal female children and adolescents (86% versus 74%). A second limitation is the subtypes of ADHD that were represented in the study sample. According to epidemiological studies, the rate of patients in HI subtype is in the range of 2%–10% (33, 34). Consistent with these proportions, HI patients represented 5.7% of the total patient sample (4/70) in our study. Since such sample sizes would violate the requirements of statistics, we did not include HI patients. However, we did include patients who were in the combined subtype, where HI symptoms coexist with AD symptoms. Future research should investigate the effect of the prescan program on children with HI subtype as well. A third limitation is that the findings from the present study were obtained from ADHD patients and control participants who went through an individualized orientation and training program before fMRI. It is formally possible that the training procedure influenced the outcome such that the effect of anxiety on compliance is masked, bringing the fMRI compliance of the extreme anxiety groups and the compliance of the ADHD and control groups to a similar level. This limitation should be treated in future factorial design studies where anxiety (low anxiety, high anxiety) and presence of the prescan program (program present, program absent) are manipulated in ADHD and control groups. Such studies will demonstrate whether it is anxiety, prescan program, or the interaction of these two that alter the fMRI compliance of ADHD patients and bring it to the level of the healthy controls.

In conclusion, in spite of their hyperactivity, impulsivity, and inattention, fMRI is possible in ADHD patients if they are systematically oriented to the MRI scanner and procedures, and trained on standard stimulation tasks. Furthermore, this outcome does not change with the level of state anxiety, demonstrating that the anxiety hypothesis of fMRI compliance is not plausible. The approaches used in our study may not be applicable during the regular working hours of a busy radiology clinic. Our findings point to the importance of providing dedicated time and/or equipment when fMRI is to be performed on children with ADHD.

Acknowledgements

We wholeheartedly thank the parents and children who volunteered to take part in this very intensive study. Their serious commitment to the lengthy data collection procedures is very much appreciated.

We thank Zeynel Baran for his contribution to data acquisition and analysis.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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